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MEDLEN & CARROLL, LLP
101 HOWARD STREET
SUITE 350
SAN FRANCISCO, CA 94105

EXAMINER	
FORD, VANESSA L	
ART UNIT	PAPER NUMBER
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/733,046	WALSH ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-46 and 55-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-46 and 55-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is responsive to Applicant's amendment and response filed December 26, 2006. Claims 34, 37, 38, 44, and 45 have been amended. Claims 1-32 and 47-54 have been cancelled. Claims 33-46 and 55-75 are under examination.

Objections/Rejections Withdrawn

2. In view of Applicant's amendment and remarks the following rejections are withdrawn.

a) Objection to the specification, paragraph 2, page 2.

b) Objection to the claim, paragraph 2, page 3.

c) rejection of claims 33-46 and 55-75 under 35 U.S.C.112, first paragraph, pages 3-6, paragraph 4.

d) rejection of claim 34 under 35 U.S.C. 112, second paragraph, page 7, paragraph 5.

e) rejection of claim 38 under 35 U.S.C. 112, second paragraph, page 7, paragraph 6.

f) rejection of claim 63 under 35 U.S.C. 112, second paragraph, page 7, paragraph 6.

g) rejection of claim 45 under 35 U.S.C. 112, second paragraph, page 8, paragraph 9.

Rejections Maintained

3. The rejection under 35 U.S.C. 112 second paragraph is maintained for claims 44 for the reasons set forth on page 7, paragraph 7 of the previous Office Action.

The rejection is reiterated below:

The rejection was on the grounds that claim 44 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 44 recites "partial fatty acid". It is unclear as to what Applicant intends? Clarification is required.

Applicant has responded to this rejection by amending claim 44 to recite "partial glycerides of fatty acids". It is unclear as to what Applicant means by "partial". The metes and bounds of "partial" cannot be ascertained. It is understood that "partial" is less than the whole but how much of the whole constitutes "partial"? Correction and/or clarification is required.

4. The rejection under 35 U.S.C. 102(b) paragraph is maintained for claims 33-37, 39-40, 42-44, 46, 55-61 and 63-75 for the reasons set forth on pages 8-9, paragraph 10 of the previous Office Action.

The rejection is reiterated below:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection was on the grounds that Blackburn et al teach a method of disinfecting (decolonizing) bacterial populations comprising topically applying to a patient a topical composition comprising nisin and one or more lantibiotics such as lysostaphin (the Abstract, column 3 and columns 11 –12, Example 7). Blackburn et al teach that the lantibiotics are present at 25 ug/ml in the compositions (column 8, Table I). Therefore the prior art teaches a topical composition comprising an antibiotic from about 0.1 to about 10.0 wt %. Blackburn et al teach the compositions of the invention comprise chelating agents such as EDTA (column 3), a carrier for topical application such as a wipe or liquid (see the Abstract, column 3 and column 5), anti-infective active agents such as such as chlorhexidine (column 3), a skin absorption promoter such as monoglycerides and fatty acids (column 4) and surfactants such as polysorbate 20 (column 4). Blackburn et al teach that composition can comprise emulsifers (column 4). Blackburn et al teach a reduction in *Staphylococcus aureus* (columns 12-14). Blackburn et al teach that the composition of the invention can be used multiple times because Blackburn et al teach that the disposable wipes comprising the composition can be used combined with cleaning and disinfecting the animals or before and after minor surgical procedures which may entail breaking the skin (column 6).

Claim limitations such as "wherein the concentration of lysostaphin in said composition is lower than the minimum inhibitory concentration of lysostaphin when used independently", "wherein the concentration of lantibiotic in said composition is lower than the minimum inhibitory concentration of lantibiotic when used independently", wherein the concentration of lysostaphin and lantibiotic in said composition is lower than the minimum inhibitory concentration of lysostaphin and lantibiotic when used independently" would be inherent in the teaching of the prior art.

Applicant Arguments

A) Applicant urges that Blackburn et al do not teach or suggest the lysostaphin is a lantibiotic. Applicant urges that lysostaphin is not a lantibiotic. Applicant urges that the Examiner's allegation that Blackburn et al (Abstract, columns 3, 11-12 and Example 7) is incorrect. Applicant urges that Blackburn et al do not teach a method of decolonizing bacterial populations. Applicant urges that there is not support in Blackburn et al to support the Examiner's allegations.

B) Applicant urges that Blackburn et al do not provide any type of protocol for generating a composition comprising lysostaphin and one or more lantibiotics nor how or if such composition could be used to decolonize bacteria at an infection site of a patient.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed December 26, 2006 have been fully considered but they are not persuasive.

A) To address Applicant's comments regarding lysostaphin being a lantibiotic, it is the Examiner's position that lysostaphin is not a lantibiotic. The claims are directed to a method of decolonizing bacterial populations. Blackburn et al teach a composition comprising nisin, subtilin, epidermin, gallidermin, cinnamycin, duramycin, ancovenia or Pep5 (lantibiotics) and teach that lysostaphin may also be employed. See column 3.

The Examiner disagrees with Applicant assertion that Blackburn et al do not teach or suggest the claimed invention.

B) To address Applicant's comments regarding Blackburn et al not providing any protocol for generating a composition comprising lysostaphin and one or more lantibiotics, it should be noted that Blackburn et al provides composition of the invention at columns 3 and 4.

To address Applicant's comment's regarding Blackburn et al not teaching a method of decolonizing bacterial populations. Blackburn et al teach a method of disinfecting (decolonizing) cow teat skin (see the Abstract). Blackburn et al teach that a method of decolonizing bacterial populations comprising topically applying to a patient in need thereof at a bacterially infected site in Example 11. Example 11 of Blackburn et al teach that cows infected with *Staphylococcus aureus* and *Staphylococcus agalactiae* and wipes of the invention were employed at the cow teat (bacterially infected site) to reduce the incidence of mastitis. Therefore, Blackburn et al teach a method of decolonizing bacterial populations.

In view of all of the above this rejection is maintained.

5. The rejection of claims 33-37, 39-40, 42-44, 46 and 55-75 under 35 U.S.C. 103(a) is maintained for the reasons set forth on pages 9-11, paragraph 11 of the previous Office Action.

The rejection is reiterated below:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection was on the grounds that the claims are drawn to a method of decolonizing populations comprising topically applying to a patient in need thereof at a bacterially infected site a topical composition comprising lysostaphin and one or more lantibiotics.

Daley et al teach a method of eliminating bacterial (*Staphlyococcus)* infections in bovine mammary glands comprising administering a composition comprising bacteriostatic peptide such as lysostaphin or nisin (column 4 and columns 11-13). Daley et al teach that the compositions of the invention contain 0.01% to about 50% by weight of the bacteriostatic peptide in the total composition (column 4). Daley et al do not teach using other lantibiotics in the method of the invention.

Blackburn et al teach compositions comprising bactericides (see the Abstract). Blackburn et al teach compositions comprising lysostaphin, nisin a chelating agent such as EDTA and a surfactant (the Abstract and columns 3-4). Blackburn et al teach that compositions may include antibiotics, copolymers and surfactants which include emulsifers and fatty acids (column 4). Blackburn et al teach that suitable carrier for the bactericides include organic solvents, buffers and polymers (column 4). Blackburn et al teach that compositions of the invention have enhanced broad range bactericide activity against bacteria such as *S. aureus* and *P. aeruginosa* (claims 18 and 19). Blackburn et al teach that the concentration of lysostaphin is about 0.1 to 100 μg/ml and the concentration of nisin is between about 0.1 and 300 100 μg/ml (column 4 and claims 20-21). Blackburn et al teach the compositions comprising lysostaphin and nisin provide broad range bactericidal activity against bacterial infections (see the Abstract and columns 6-7). Blackburn et al teach that bactericidal activity and the overall speed of

bactericidal activity is enhanced when two bacteriocins are combined in one composition (column 2). Blackburn et al teach that the compositions of the invention can be formulated into lotion and ointments (column 3). Therefore, the prior art necessarily teaches the claim limitation "wherein said emulsifier is an inverse emulsion of polyacrylamide in liquid paraffin.

Claim limitations regarding how many times the composition is applied to the infected site would be a matter of optimizing experimental parameters (see claims 68-71).

It would be *prima facie* obvious at the time the invention was made to modify he method of eliminating bacterial infections as taught by Daley et al to administer to a patient with a bacterial infection (*S. aureus* and *P. aeruginosa* infections) because Blackburn et al discloses that a composition comprising lysostaphin and nisin provide broad range bactericidal activity against bacterial infections and the overall speed of bactericidal activity is enhanced when two bacteriocins are combined in one composition.

Applicant's Arguments

A) Applicant urges that the cited references, individually or combined do not suggest how to modify compositions and methods disclosed therein in order to produce the claimed invention. Applicant urges that the cited references do not provide a reasonable expectation of success for carrying out the claimed invention. Applicant urges that they disagree with the Examiner's allegation that it would be *prima facie* obvious at the time the invention was made to modify the method of eliminating bacterial infection as taught by Daley et al ('612) to administer to a patient with a bacterial infection because Blackburn et al ('163) disclose that a composition comprising lysostaphin and nisin provide broad range bactericidal activity against bacterial infections.

B) Applicant urges that the cited references do not provide any type of protocol for generating a composition comprising lysostaphin and one or more lantibiotics nor how

or if such composition could be used to decolonize bacteria at an infection site of a patient.

C) Applicant urges that no guidance is provided by either reference as to whether a topical composition comprising lysostaphin, nisin and a surfactant or a chelating agent or carvacol would be effective at decolonizing bacterial populations present within an infected site. Applicant urges that no guidance is provided by either reference as to whether a topical composition comprising lysostaphin a lantibiotic would be effective at decolonizing bacterial populations present within an infected site of a patient.

D) Applicant urges that Patent ('162) teach that addition of various reagents to a composition comprising lysostaphin and nisin can inhibit their bactericidal properties. Applicant urges that for example, Patent ('162) teach that lysostaphin in an oil base (peanut base) loses its bactericidal capacity and the EDTA can inhibit the activity of nisin.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed December 26, 2006 have been fully considered but they are not persuasive.

A) In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re*

Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Daley et al teach a method of eliminating bacterial (*Staphlyococcus)* infections in bovine mammary glands comprising administering a composition comprising bacteriostatic peptide such as lysostaphin or nisin. Daley et al do not teach using other lantibiotics in the method of the invention. However, Blackburn et al teach compositions comprising lysostaphin and lantibiotics such as nisin and chelating agents and surfactants. One would be motivated to use a composition comprising lysostaphin, nisin, chelating agents and surfactants in a method to decolonize bacterial populations because Daley et al teach a composition comprising lysostaphin or nisin can eliminate bacterial (*Staphlyococcus)* infections in bovine mammary glands. and Blackburn et al teach that composition comprising lysostaphin, nisin, chelating agents and surfactants enhance broad range bactericides and are bactericidal in both gram-negative and gram-positive organisms (column 4).

B) To address Applicant's comments regarding the cited references not providing any protocol for generating a composition comprising lysostaphin and one or more lantibiotics, it should be noted that Blackburn et al ('163) provides compositions comprising lysostaphin, nisin, chelating agents and surfactants. See columns 3-4.

C) To address Applicant's arguments comprising that no guidance is provided by either reference as to whether topical administration of a composition comprising lysostaphin, nisin, a surfactant and a chelating agent or carvacol would be effective at decolonizing bacterial populations at a target site, it should be noted that Blackburn et al ('163) teach that the composition of the invention used for broad range treatment against bacterial infections can be incorporated into ointments, wound dressings,

disinfectant scrubs, wipes and lotions (column 3). Therefore, one of skilled in the art would reasonably conclude that the compositions of the invention would be effective at decolonizing bacterial populations at bacterially infected sites by topical administration.

D) It should be noted that the references used in this rejection are Daley et al *(U.S. Patent No. 5,342,612 published August 1994)* and Blackburn et al *(U.S. Patent No. 4,980, 163 published December 25, 1990)*. No patent ('162) was used. It appears that Applicant may be referring to Daley et al *(U.S. Patent No. 5,342,612). However,* there is no disclosure of peanut oil nor is there a disclosure stating that lysostaphin loses its bactericidal capacity and the EDTA can inhibit the activity of nisin.

In view of all of the above this rejection is maintained.

New Grounds of Rejection

Specification

6. "WO 03/82124" recited in the specification at page 12, line 25 is incorrect. This document should be "WO 03/082184". Further, the attempt to incorporate subject matter in this application by reference to WO 03/82184 is ineffective. This attempt to incorporate by reference is ineffective because MPEP 608 states:

An application as filed must be complete in itself in order to comply with 35 U.S.C. 112. Material nevertheless may be incorporated by reference, Ex parte Schwarze, 151 USPQ 426 (Bd. Ape. 1966). An application for a patent when filed may incorporate "essential material" by reference to (1) a U.S. patent, (2) a U.S. patent application publication, or (3) a pending U.S. application, subject to the conditions set forth below.

"Essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112). In any application which is to issue as a U.S. patent, essential material may not be incorporated by reference to (1) patents or applications published by foreign countries or a regional patent office, (2) non-patent publications, (3) a U.S. patent or application which itself incorporates "essential material" by reference, or (4) a foreign application.

The incorporation by reference will not be effective until correction is made to comply with 37 CFR 1.57(b), (c), or (d). If the incorporated material is relied upon to meet any outstanding objection, rejection, or other requirement imposed by the Office, the correction must be made within any time period set by the Office for responding to the objection, rejection, or other requirement for the incorporation to be effective. Compliance will not be held in abeyance with respect to responding to the objection, rejection, or other requirement for the incorporation to be effective. In no case may the correction be made later than the close of prosecution as defined in 37 CFR 1.114(b), or abandonment of the application, whichever occurs earlier. Any correction inserting material by amendment that was previously incorporated by reference must be accompanied by a statement that the material being inserted is the material incorporated by reference and the amendment contains no new matter. 37 CFR 1.57(f).

Claim Rejections - 35 USC § 112

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 34 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses that lysostaphin encompasses any enzyme or anti-staphylococcal agent having proteolytic activity *in vitro* and *in vivo* against pentaglycine-containing bridges in the cell wall peptidoglycan of staphylocooci (page 12). However, claim 34 is directed to the method of claim 33 wherein topical composition comprises from about 0.10 to about 10.0 wt% of lysostaphin selected from the group consisting of wild-type lysostaphin, a lysostaphin mutant wherein said lysostaphin mutant lacks the first two alanine amino acids of the full length lysostaphin amino acid sequence and recombinant lysostaphin.

The instant specification has failed to provide a structure for the lysostaphin mutants used in the claimed method. The recitation "lacks the first two alanine amino acids of the full length amino acid sequence" does not provide structure for the lyostaphin mutants used in the claimed method. None of these sequences meet the

written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

It should be noted that the full-length lysostaphin can lack the first two alanine amino acids and also have modification along the rest of its amino acids sequence. The instant specification has not taught or disclosed the structure of this polypeptide nor has the instant specification disclosed what changes or modifications can be made to the polypeptide and the polypeptide retains the intended biological function. The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2datl966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

The species specifically recited in the claims (lacks the first two alanine amino acids of the full length amino acid sequence) is not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) The instant specification has not provided a structure for the lysostaphin mutant recited in the claims.

Additionally, Applicant has incorporated by reference in the instant specification "essential material" (e.g. the structure of the lysostaphin mutants used in the claimed method). It should be noted that newly filed applications obviously failing to disclose an invention with the clarity required are discussed in MPEP § 702.01. A disclosure in an application, to be complete, must contain such description and details as to enable any

person skilled in the art or science to which the invention pertains to make and use the invention as of its filing date. In re Glass, 492 F.2d 1228, 181 USPQ 31(CCPA 1974).

An application as filed must be complete in itself in order to comply with 35 U.S.C. 112. Material nevertheless may be incorporated by reference, Ex parte Schwarze, 151 USPQ 426 (Bd. App. 1966). An application for a patent when filed may incorporate "essential material" by reference to (1) a U.S. patent, (2) a U.S. patent application publication, or(3) a pending U.S. application, subject to the conditions set forth below. "Essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112). In any application which is to issue as a U.S. patent, essential material may not be incorporated by reference to (1) patents or applications published by foreign countries or a regional patent office, (2) non-patent publications, (3) a U.S. patent or application which itself incorporates "essential material" by reference, or (4) a foreign application.

In view of all of the Applicant have not meet satisfied the written description requirement set forth under 35 U.S.C. 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claim 41 recites "wherein said topical composition further comprises at least one of bacitracin and neomycin" which renders the claim indefinite by reciting improper Markush language. It is unclear as to what Applicant is referring. Does Applicant intend that one bacitracin and one neomycin is contained in the composition or does Applicant intend that one bacitracin or one neomycin is contained in the composition? Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See Ex parte Markush, 1925 C.d. 126 (Comm'r Pat. 1925).

9. Claim 45 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite by reciting improper Markush language. It is unclear as to what Applicant is referring. It is unclear as to what components are in the composition besides lysostaphin and one or more lantibiotics? Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See Ex parte Markush, 1925 C.d. 126 (Comm'r Pat. 1925).

10. Claim 63 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 63 recites "hard fat". It is unclear as to what Applicant intends? Clarification is required.

Claim 45 is included in the art rejection below because it is unclear as to which components besides lysostaphin and one or more lantibiotics are included in the composition used in the claimed method. See rejection under 35 U.S.C. 112 second paragraph, item 9 above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 33-40, 42-46, 55-61 and 63-75 are rejected under 35 U.S.C. 103(a) as unpatentable over Blackburn et al (*U.S. Patent 5,762,948 published June 9, 1998)* in view of Gasson et al (*U.S. Patent 6,448,034 B1 published September 10, 2002).*

The claims are drawn to a method of decolonizing populations comprising topically applying to a patient in need thereof at a bacterially infected site a topical composition comprising lysostaphin and one or more lantibiotics.

Blackburn et al teach a method of disinfecting (decolonizing) bacterial populations comprising topically applying to a patient a topical composition comprising nisin and one or more lantibiotics such as lysostaphin (the Abstract, column 3 and columns 11 –12, Example 11). Blackburn et al teach that the lantibiotics are present at 25 ug/ml in the compositions (column 8, Table I). Therefore the prior art teaches a topical composition comprising a antibiotic from about 0.1 to about 10.0 wt %. Blackburn et al teach the compositions of the invention comprise chelating agents such as EDTA (column 3), a carrier for topical application such as a wipe or liquid (see the Abstract, column 3 and column 5), anti-infective active agents such as such as

chlorhexidine (column 3), a skin absorption promoter such as monoglycerides and fatty acids (column 4) and surfactants such as polysorbate 20 (column 4). Blackburn et al teach that composition can comprise emulsifers (column 4). Blackburn et al teach a reduction in *Staphylococcus aureus* (columns 12-14). Blackburn et al teach that the composition of the invention can be used multiple times because Blackburn et al teach that the disposable wipes comprising the composition can be used combined with cleaning and disinfecting the animals or before and after minor surgical procedures which may entail breaking the skin (column 6).

Blackburn et al do not teach using nisin variants nisin variant H27K and nisin variant H31K.

Gasson et al teach nisin variants nisin variant H27K and nisin variant H31K. Gasson et al teach that variant nisins which have improved properties compared with natural nisA nisin are preferred, for example those variant nisins which have more potent antimicrobial activity or that have greater resistance to hydrolysis or degradation when added to foodstuffs (column 6). Claim limitations such as "wherein the concentration of lysostaphin in said composition is lower than the minimum inhibitory concentration of lysostaphin when used independently", "wherein the concentration of lantibiotic in said composition is lower than the minimum inhibitory concentration of lantibiotic when used independently", wherein the concentration of lysostaphin and lantibiotic in said composition is lower than the minimum inhibitory concentration of lysostaphin and lantibiotic when used independently" would be necessarily taught by the prior art. Regarding the specific concentrations listed in the instant claims, MPEP

2144.05 states, "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler,* 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)."

It would be *prima facie* obvious at the time the invention was made to modify the method of decolonizing bacterial infections as taught by Blackburn et al to administer to

a patient with a bacterial infection (*S. aureus* and *P. aeruginosa* infections) a composition comprising lysostaphin and nisin variants H27K or H31K because Blackburn et al teach that compositions comprising lysostaphin and nisin can disinfect cow teat skin and reduce bacterial infection (Abstract and Example 11) and Gasson et al discloses that Gasson et al teach that variant nisins which have improved properties compared with natural nisA nisin are preferred, for example those variant nisins which have more potent antimicrobial activity. It would be expected absent evidence to the contrary that a composition comprising lysostaphin and nisin variants H27K or H31K would be effective in decolonizing a bacterial population, thereby by reducing bacterial infection.

12. Claim 41 is rejected under 35 U.S.C. 103(a) as unpatentable over Blackburn et al and Gasson et al as applied to claims 33-40, 42-46, 55-61 and 63-75 above and further in view of Krieger et al (*U.S. Patent No. 6,503,881 B1 published January 7, 2003).*

Claim 41 is drawn to the method of claim 33 wherein said topical composition further comprises at least one of bacitracin and necomycin".

The teachings of Blackburn et al and Gasson et al have been described previously.

Blackburn et al and Gasson et al do not teach the claim limitation "the method of claim 33 wherein said topical composition further comprises at least one of bacitracin and necomycin".

Kreiger et al teach bacitracin suppresses colonization of (*Staphylococcus aureus)* (column 37). Kreiger et al teach compositions and methods for treating infections, especially bacterial infections (see the Abstract).

It would be *prima facie* obvious at the time the invention was made to modify the method of decolonizing bacterial infections as taught by Blackburn et al to administer to a patient with a bacterial infection (*S. aureus* and *P. aeruginosa* infections*)* a composition comprising lysostaphin, nisin variants H27K or H31K and bacitracin because Blackburn et al teach that compositions comprising lysostaphin and nisin can disinfect cow teat skin and reduce bacterial infection, Gasson et al discloses that Gasson et al teach that variant nisins which have improved properties compared with natural nisA nisin are preferred, for example those variant nisins which have more potent antimicrobial activity and Krieger et al teach that bacitracin suppresses colonization. It would be expected absent evidence to the contrary that a composition comprising lysostaphin, nisin variants H27K or H31K and bacitracin would be effective in decolonizing a bacterial population, thereby by reducing bacterial infection.

Status of Claims

13. No claims allowed.

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Vanessa L. Ford
Biotechnology Patent Examiner
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